REMARKS

In response to the Office Action, Applicants have amended some of the application claims, as listed above, and canceled (without prejudice to or disclaimer thereof) other claims as recited above. Applicants specifically reserve the right to prosecute the cancelled subject matter in subsequent continuation or divisional applications. After entry of the claim amendments and cancellations offered herein, claims 1-2, 9-40, 53-63, 65-71, 74-112 will be pending in the application.

Claim 1 has been amended to replace the original recitation of polysaccharides with a recitation of pectins having a degree of methylation of less than 50%, support for which can be found in the specification at page 23 and original claim 8. Independent claims 1 and 53 have been amended to recite a particular class of biologically derived physiologically active agents (peptides, proteins, vaccines comprising one or more antigens, live cells, dead cells in whole or in part, or viruses in whole or in part), and support for these amendments can be found in the specification *inter alia*, at pages 8 and 24, and original claims 18-21, and 72-76. Independent claims 1, 53, and 111 have been amended to recite that the one or more physiologically active agents, and the one or more pectins form a solid mixed composition phase wherein the agent and the polysaccharide are mixed on the molecular level and the one or more solid gel inducing compositions are distinct solid phases. Support for this amendment can be found at page 26 and original claim 32. Accordingly, the claim amendments recited above do not introduce new matter, and should be entered.

Rejections Under 35 U.S.C. § 112, 2nd Paragraph

Claims 32 and 33 were rejected under 35 U.S.C. § 112, 2nd paragraph because inclusion of the word "intimately" was alleged to have rendered those claims indefinite. While Applicants do not concede the validity of the rejection, in the interests of facilitating prosecution Claim 32 has been canceled, but the text of claim 32 has been amended into claims 1, 53, and 111, but with the deletion of the word "intimately."

One of ordinary skill in the art would readily understand the meaning of the new clause of amended claims 1, 53, and 111, i.e. "the one or more pectins form a solid mixed composition phase wherein the agent and the polysaccharide are mixed on the molecular level." This is simply a description of a solid mixture wherein the pectins and agent are not present as a physical mixture of micro-crystals of each of the separate mixtures, but rather are both present in a solid phase wherein the individual pectin and agent molecules are mixed within the solid phase. Moreover, the specification page 26 discloses the unremarkable proposition that such solid mixtures "on the molecular level" can often be formed by simply dissolving the physiologically active agent and the polysaccharide (pectin) to form a solution in a suitable liquid carrier, and then the liquid carrier removed by any of a variety of means, to form mixture of the components on the molecular level in a solid form.

Applicants accordingly assert that the removal of the word "intimately" overcomes any allegation of indefiniteness, and the rejection should be withdrawn.

REJECTIONS FOR ANTICIPATION AND/OR OBVIOUSNESS OVER THE PRIOR ART

The examiner has initiated an entirely new series of rejections, based on new prior art references, i..e. U.S. Patent No. 5,612,053 to Baichwal et al (hereinafter "Baichwal"), in view of

U.S. Patent No. 6,310,089 to Watts et al (hereinafter "Watts"), U.S. Patent No. 5,929,051 to Ni et al (hereinafter "Ni'), U.S. Patent No. 6,518,239 to Kuo et al (hereinafter "Kuo"), Gordon et al (U.S. Patent No. 2,629,665, hereinafter "Gordon"), .and/or Mizushima et al (U.S. Patent No. 5,942,242, hereinafter "Mizushima").

A number of the original claims directed to solid pharmaceutical compositions comprising anionic polysaccharides were rejected for anticipation over Baichwal, but the Examiner conceded on page 5 that Baichwal "did not disclose pectin as such a polysaccharide." All of applicants' claims have been amended to recite pectins and/or pectic substances, therefore none of Applicants' amended claims are anticipated by Baichwal, and the rejection for anticipation by Baichwal has been overcome and should be withdrawn.

The Office Action then rejected Applicants' previously pending claims for obviousness under 35 U.S.C. §103(a) over Baichwal, in view of several other secondary references. Watts is recited for its alleged teachings of the use of pectins in powdered compositions for the controlled release of drugs. Ni is cited for its alleged teachings re the suitability of the use of certain pectins with low degrees of methylation in compositions for the controlled release of a physiologically active agent to an animal. The Office Action recites Kuo for its alleged teachings of the delivery of vaccines by inhalation of dry powders. Gordon is cited for its alleged teachings of the use of calcium phosphate to cause a pectin to form a gel. The Office Action also cites Mizushima for its alleged teachings of the use of various thickening agents as additives to inhalable powders, because they increased adherence to nasal mucosa.

Applicants concede that pectins, vaccines, thickeners, and calcium gel inducing reagents have all been used in the prior art as components of solid pharmaceutical compositions for

controlled release of drugs. Applicants do not agree with the allegations of the Office Action, and reliance on MPEP 2144.06 for a proposition that simply because each of those ingredients has been previously used as a component of a previous solid composition for the controlled release of a physiologically active agent, that the use any such ingredient cited in the prior art, in conjunction with any other combination of such known agents, is *prima facie* obvious. To the contrary, it is elementary patent law, and has very often been stated by the Federal Circuit, that most or all newly patentable inventions arise from new and non-obvious combinations of previously known elements.

Applicants' amended claims represent such a patentable combination of elements. In order to arrive at the combination of elements recited in Applicant's independent claims, one of ordinary skill in the art would have to make the multiple selections of elements from among Baichwals' many alternative disclosures in order to arrive at a formulation of a solid polysaccharide composition comprising a solid mixture of a polysaccharide gum and one of the biologically derived physiologically active agent recited in Applicant's amended claims, wherein the composition was formulated as a solid mixture of components rather than a physical composite of separate ingredients, and wherein the composition is not "pre-gelled" as formulated, and having appropriate particle sizes ,but the particles would in fact form a gel "in-situ" when contacted with a tissue or body fluid of an animal. Moreover, even if one of ordinary skill in the art were to *arguendo* make the multiple selections from among the teachings of Baichwal that would be necessary to arrive at such a solid composition, would still be necessary to make multiple further selections and/or modifications in order to additionally arrive at the use of pectins having a low degree of methylation, and/or cationic cross-linking agents for those

pectins, and/or thickers, in order to produce gels "in-situ" when the modified composition was contacted with a tissue or body fluid. It is far from obvious from the cited prior art to make the necessary number of specific selections and/or modifications that would be required to arrive at the combination of elements recited in Applicants amended claims. Accordingly, it is not *prima facie* obvious to one of ordinary skill in the art to select from the cited prior art the particular combinations of elements recited in Applicants' claims.

Moreover, Applicants contend that the specific compositions recited in their amended claims exhibit many unexpected advantages and/or overcome many previously unsolved problems in the art, and therefore establish their patentability. Many physiologically active biological agents, such as those recited in Applicants' amended claims, are typically formulated as liquids that require cold storage, and/or are administered by injection or other means, because oral or nasal administration is highly inefficient or totally ineffective. In contrast, Applicants' claimed solid "in-situ gelling" compositions are formulated so that the large biological agents, which are unstable in solution at room temperature, are stabilized when formulated in the form of Applicant's claimed solid mixture compositions, and exhibit unexpectedly extended shelf-lives when stored at room temperature. See specification page 23. Moreover, once Applicants' claimed solid compositions are applied to nasal or other mucosal surfaces, they become very finely dispersed on those mucosal surfaces, and then gel "in-situ" to produce a highly bio-adhesive gel that adheres unusually well to nasal mucosal surfaces. Moreover, by the selection of the molecular weight and/or degree of methylation of the pectins, and/or addition of additional ingredients, such as the gel inducing compositions comprising divalent or multi-valent cations (claim 1), or excipients (claim 27), thickeners (claim 29), the rate of formation and amount and

degree of cross-linking of the gel that is formed "in-situ" on the mucosal surface can be varied so as to optimize the rate of initial and long-term release of the delicate biological agents being delivered to the surfaces. See Examples 27 and 28. As discussed in Applicants' specification at pages 29 and 30, previous attempts to efficiently apply biological agents such as proteins and/or vaccines to mucosal surfaces have been previously unsuccessful because of the rapid clearance of the compositions from the nasal mucosa. Moreover, it is clear from Example 29 that nasal delivery of vaccine antigens to the nasal mucosal membranes of mice results in dramatic increases in resulting IgA anti-body titers, as compared to similar nasal administrations with simple liquid formulations.

Accordingly, even if the Examiner could *arguendo* establish the prima facie obviousness of making the particular selections of elements recited in Applicants' claims, which Applicants deny, because of the unexpected advantages of Applicants' claimed compositions for the controlled release and effective administration of the recited biologically-related physiologically active agents, Applicants' claims are non-obvious and patentable over the prior art, and Applicants' claims should be allowed.

CONCLUSION

In view of the claims amendments and arguments recited above, Applicants respectfully submit that all outstanding objections and rejections stated in the Office Action have been overcome and should be withdrawn. Accordingly, the application is believed to be in condition for allowance and Applicants respectfully request issuance of a Notice of Allowance.

Attached herewith is a Request for a Three Month Extension of Time, and a Credit Card Payment Form PTO-2038 authorizing payment in the amount of $510.00 for the extension of

time fee for a small entity under 37 C.F.R. § 1.(a)(2). This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this document and any documents referenced herein as being enclosed herein are being deposited with the United States Postal Service as first class mail in an envelope addressed to: MAIL STOP AMENDMENT, Commissioner for Patents, P. O. Box 1450, Alexandria, VA, 22313-,1450, on the date indicated below.

Mark A. Murphy, Ph.D. Date April 30, 2007